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Novel C_2-Symmetric Planar Chiral Diphosphine Ligands and Their Application in Pd-Catalyzed Asymmetric Allylic Substitutions

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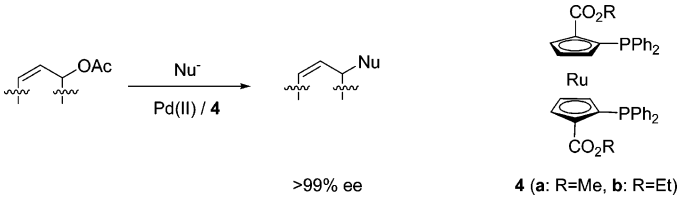

Novel C_2-symmetric diphosphine ligands possessing only the planar chirality of ruthenocene, 1,1′-bis-(diphenylphosphino)-2,2′-disubstituted-ruthenocenes (**4**), were prepared. With this kind of ligands, excellent enantioselectivity and especially highly catalytic activity in palladium-catalyzed asymmetric allylic substitutions of *rac*-1,3-diphenyl-2-propenyl acetate (**9**) were observed, compared to their ferrocene analogues **1**. Good enantioselectivity and highly catalytic activity were also obtained with **4** in palladium-catalyzed asymmetric allylic substitutions of cyclohexen-1-yl acetate (**12**). Further study on the effect of R in ester group on enantioselectivity of **4** showed an opposite trend compared with their ferrocene analogues **1** in asymmetric allylic substitutions. For ruthenocene ligands **4**, the one with the smaller R in the ester group gave higher enantioselectivity for the palladium-catalyzed asymmetric allylic substitutions of **9**, while a converse trend had been observed with **1**. However, for the palladium-catalyzed asymmetric allylic substitutions of **12**, ligand **4** with a larger R in the ester group resulted in somewhat higher enantioselectivity but still an opposite trend with ligand **1**. The X-ray diffraction study of crystal structures of **4** and **1** with Pd(II) was carried out and showed that the enantioselectivity was correlated to the twist angle existing in the palladium complex.

Introduction

In the last few decades, tremendous progress has been made in the design of new chiral ligands for the development of efficient metal-catalyzed asymmetric transformations.[1] Of the various chiral ligands reported, diphosphines are the most popular in asymmetric catalysis, due mainly to their stability and outstanding ability to form highly active and selective complexes with transition metals.[2]

Ferrocene-based planar chiral ligands have received intensive attention, and many kinds of planar chiral ferrocene ligands have been developed recently.[3] Meanwhile, C_2-symmetric chiral

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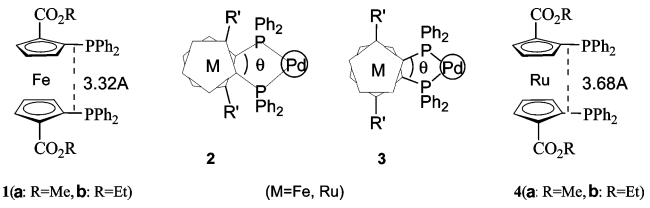

FIGURE 1. Structure of **1** and **4** and their complexation with palladium.

ferrocene ligands, especially those with only planar chirality, have recently gained much attention since the pioneering work reported by the Ikeda group.[4] It was also known that an asymmetric reaction environment such as dihedral angle in some C_2-symmetric axially chiral diphosphine ligands is essential for attaining high enantioselectivity in asymmetric catalysis.[5] During the development of the C_2-symmetric planar chiral ligands, we were interested to see if varying the twist angle of the two Cp rings upon complexation of the ligands with a metal would have an effect on the asymmetric catalytic reaction (Figure 1).

It was reported that C_2-symmetric planar chiral diphosphine ferrocene ligands **1** were efficient for Pd-catalyzed asymmetric allylic alkylation (Figure 1).[4a,e] When **1a** was coordinated with Pd(II), only configuration **2** of the complex was formed and no **3** was found at all. We conceived that the twist angle θ of **2** could have a nonneglectable effect on the catalytic activity and enantioselectivity. On the one hand, θ could be changed via changing metal atom Fe to Ru between the two Cp rings because of the different distances of two Cp rings in ferrocene and ruthenocene backbone. On the other hand, it could be also changed by changing R′ groups on the Cp rings (Figure 1, configuration **2**). For this purpose we are interested in developing a new type of C_2-symmetric planar chiral diphosphine ruthenocene ligands. To the best of our knowledge, there are few reports on the development of chiral ruthenocene ligands.[6] Thus, we report herein the synthesis and crystal structure study of novel ruthenocenediphosphine ligands **4** and their application to Pd-catalyzed asymmetric allylic substitutions, by comparing with their ferrocene analogues **1**.

Results and Discussion

Synthesis of Ester Amide (4). Ligands **4** can be easily prepared from **5**[6c] by the transformation of the oxazoline moieties in the molecule by the method reported (Scheme 1).[4e] Thus, treatment of **5** with trifluoroacetic acid in aqueous THF caused ring-opening of the oxazoline moiety to give an unstable ammonium salt. This ammonium salt was acetylated with acetic anhydride without isolation in the presence of pyridine to give ester amide **6** in 83% yield. Transesterification of **6** with methanolic sodium methoxide at room temperature for 24 h gave ligand **4a** in 75% yield. Ligand **4b** was also prepared from **6** by a similar procedure with a yield of 74%.

Catalytic Test of Palladium-Catalyzed Asymmetric Allylic Alkylation. With the novel C_2-symmetric planar chiral P,P-chelating ligands **4** in hand, we first tried to apply them in palladium-catalyzed asymmetric allylic alkylation of *rac*-1,3-diphenyl-2-propenyl acetate (**9**) with dimethyl malonate, which is a classic substrate for many new kinds of ligands to test their asymmetric catalytic behavior.[7] The results were summarized in Table 1.

The influence of reaction conditions upon the allylic alkylation was taken into account. First of all, the effect of the solvent on the catalytic reaction was examined with **4a** (Table 1, entries 1−5). Dichloromethane was selected as the best one according to the chemical yield and the enantioselectivity. The addition of NaOAc also affected the enantioselectivity. In the absence of NaOAc, 83.6% ee was obtained and the enantioselectivity was enhanced to 91.0% ee when it was used (Table 1, entries 1 and 6). The temperature also affected the enantioselectivity, and up to 95.7% ee was obtained at −25 °C with **4a** (Table 1, entries 7−9). It was further shown that the R in the ester group has an effect on this asymmetric synthesis with **4a** methyl ester leading to higher enantioselectivity compared with **4b** ethyl ester (Table 1, entries 8 and 10).

Compared with ferrocene ligands **1**, much higher catalytic activity was obtained with ruthenocene ligands **4** for this asymmetric allylic alkylation. The reactions could be completed within 30 min at room temperature in suitable solvents and not more than 2 h even at −25 °C (Table 1, entries 8 and 10).

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SCHEME 1. Synthesis of Ligands 4

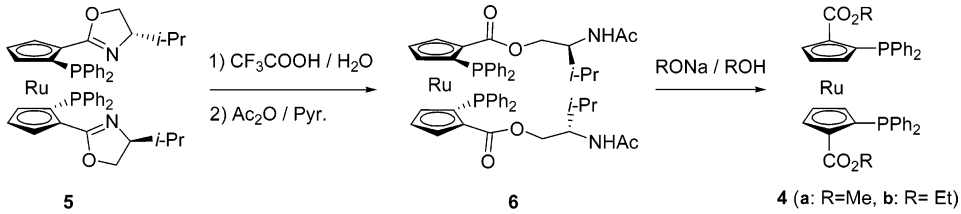
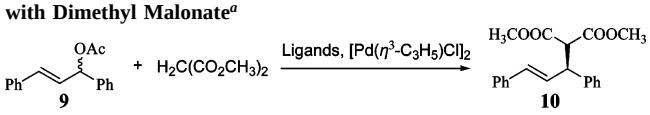


TABLE 1. Allylic Substitution of 1,3-Diphenyl-2-propenyl Acetate with Dimethyl Malonate[a]



entry	ligand	*T*/°C	time/h	solvent	ee (%)[b,c]/ yield (%)
1	**4a**	25	0.5	CH_2Cl_2	91.0/99
2	**4a**	25	0.5	DMF	87.2/99
3	**4a**	25	0.5	CH_3CN	87.1/99
4	**4a**	25	4	toluene	74.4/98
5	**4a**	25	8	THF	71.8/92
6[d]	**4a**	25	0.5	CH_2Cl_2	83.6/99
7	**4a**	0	1	CH_2Cl_2	92.4/99
8	**4a**	−25	2	CH_2Cl_2	95.7/99
9	**4a**	−78	7	CH_2Cl_2	94.1/99
10	**4b**	−25	2	CH_2Cl_2	92.9/99
11[e]	**1a**	25	1	CH_2Cl_2	86/>90
12[e]	**1b**	25	3	CH_2Cl_2	91/>90
13[e]	**1a**	−25	72	CH_2Cl_2	88/>90

[a] Molecular ratio: $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$/NaOAc/ligand/substrate/BSA/$H_2C(CO_2Me)_2$ = 2.5/4/6.0/200/600/600. Reactions were conducted under nitrogen. The catalysts were prepared by treating $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ with ligands in suitable solvent at 20 °C for 1 h before use. [b] Determined by the HPLC, using chiral OD-H column. [c] The absolute configurations were assigned as *S* through comparison of the sign of specific rotations with the literature data.[8] [d] No NaOAc was used. [e] See ref 4e.

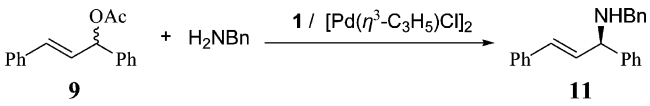
However, 72 h was required for the completion of the reaction when ferrocene ligand **1a** was used at −25 °C (Table 1, entry 13). On the other hand, it was observed that the enantioselectivity varied with the metals between the two Cp rings. When ferrocene ligand **1a** was used as ligand under −25 °C, 88% ee was obtained and the enantioselectivity was raised to 95.7% ee if ruthenocene **4a** was used in the same conditions (Table 1, entries 8 and 13). It was shown that the group R in the ester group also had an effect on the asymmetric catalysis of both **4** (Table 1, entries 8 and 10) and **1** (Table 1, entries 11 and 12) but with an opposite trend.

Catalytic Test of Palladium-Catalyzed Asymmetric Allylic Amination with 1. The applications of this kind of ligands were extended to the asymmetric allylic amination of **9** with benzylamine. For comparison, **1** was used first and showed excellent asymmetric induction in this model reaction with high yields (Table 2).

The solvents showed some effect on this reaction (Table 2, entries 1−6). Toluene was selected as the optimal one to examine the effect of temperature on this asymmetric reaction. It could be concluded that the temperature (Table 2, entries 6−9) and the R in the ester group (Table 2, entries 7 and 10) had a little effect on the enantioselectivity. Up to 99.1% ee was obtained with **1b** at 0 °C in toluene.

Catalytic Test of Palladium-Catalyzed Asymmetric Allylic Amination with 4. First, **4** was used in the asymmetric allylic amination with the optimal conditions mentioned above (Table 2, entry 7), but the results were unpleasing (Table 3, entries 1 and 2). Thus, the influence of reaction conditions of **4a** upon the asymmetric catalytic reaction was investigated. Dichloromethane was found to be the optimal solvent for this reaction according to the chemical yield and the enantioselectivity (Table

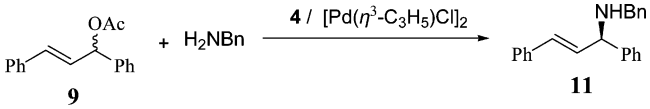
TABLE 2. Allylic Substitution of 1,3-Diphenyl-2-propenyl Acetate with Benzylamine[a]



entry	ligand	*T*/°C	*t*/h	solvent	ee (%)[b,c]/ yield (%)
1	**1a**	20	1	CH_2Cl_2	94.5/99
2	**1a**	20	1	$(CH_2Cl)_2$	94.2/99
3	**1a**	20	24	THF	94.3/78
4	**1a**	20	7	DMF	94.5/99
5	**1a**	20	1	CH_3CN	93.8/99
6	**1a**	20	2	toluene	96.8/99
7	**1a**	0	4	toluene	98.7/99
8	**1a**	−25	12	toluene	98.6/92
9	**1a**	−78	48	toluene	97.0/89
10	**1b**	0	4	toluene	99.1/99

[a] Molecular ratio: $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$/ligand/substrate/benzylamine = 1/2.2/100/300. Reactions were conducted under nitrogen. The catalysts were prepared by treating $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ with ligands in suitable solvent at 20 °C for 1 h before use. [b] Determined by the HPLC, using chiral OJ-H column. [c] The absolute configurations were assigned as *R* through comparison of the sign of specific rotations with the literature data.[9]

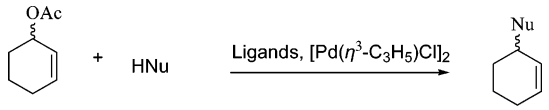
TABLE 3. Allylic Substitution of 1,3-Diphenyl-2-propenyl Acetate with Benzylamine[a]



entry	ligand	*T*/°C	*t*	solvent	ee (%)[b,c]/ yield (%)
1	**4a**	0	48 h	toluene	93.8/73
2	**4b**	0	48 h	toluene	89.0/68
3	**4a**	20	20 min	CH_2Cl_2	94.2/99
4	**4a**	20	20 min	$(CH_2Cl)_2$	91.4/99
5	**4a**	20	7 h	THF	95.0/89
6	**4a**	20	20 min	DMF	93.5/99
7	**4a**	20	20 min	CH_3CN	91.9/99
8	**4a**	20	20 h	toluene	94.9/76
9	**4a**	0	40 min	CH_2Cl_2	97.6/99
10	**4a**	−25	1.5 h	CH_2Cl_2	99.2/99
11	**4a**	−78	10 h	CH_2Cl_2	97.0/84
12	**4b**	−25	3 h	CH_2Cl_2	99.0/99
13	**5**	20	1.5 h	CH_2Cl_2	87.2/99

[a] Molecular ratio: $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$/ligand/substrate/benzylamine = 1/2.2/100/300. Reactions were conducted under nitrogen. The catalysts were prepared by treating $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ with ligands in suitable solvent at 20 °C for 1 h before use. [b] Determined by the HPLC, using chiral OJ-H column. [c] The absolute configurations were assigned as *R* through comparison of the sign of specific rotations with the literature data.[9]

TABLE 4. Allylic Substitution of Cyclohexen-1-yl Acetate with Dimethyl Malonate[a] and Benzylamine[b]



12 **13**

(**a**: Nu= $HC(CO_2CH_3)_2$, **b**: Nu= NHBn)

entry	ligand	HNu	*T*/°C	*t*/h	solvent	ee (%)[c,d]/ yield (%)
1	**4a**	$H_2C(CO_2CH_3)_2$	−25	0.5	CH_2Cl_2	78.4/93
2	**4b**	$H_2C(CO_2CH_3)_2$	−25	0.5	CH_2Cl_2	79.8/94
3	**4a**	$BnNH_2$	−25	1.5	CH_2Cl_2	60.5/86
4	**4b**	$BnNH_2$	−25	2	CH_2Cl_2	66.7/89
5[e]	**1a**	$H_2C(CO_2CH_3)_2$	0	0.5	CH_2Cl_2	81/>90
6[e]	**1b**	$H_2C(CO_2CH_3)_2$	0	0.5	CH_2Cl_2	77/>90
7	**1a**	$BnNH_2$	0	2	toluene	77.4/88
8	**1b**	$BnNH_2$	0	2	toluene	69.3/92

[a] Molecular ratio: $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$/NaOAc/ligand/substrate/BSA/$H_2C(CO_2Me)_2$ = 2.5/4/6.0/200/600/ 600. [b] Molecular ratio: $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$/ligand/substrate/benzylamine =1/2.2/100/300. Reactions were conducted under nitrogen. The catalysts were prepared by treating $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ with ligands in suitable solvent at 20 °C for 1 h before use. [c] Determined by the HPLC, using chiral AD-H column. [d] The absolute configurations were assigned as *R* through comparison of the sign of specific rotations with the literature data.[11] [e] See ref 4e.

3, entries 3−8). The temperature also affected the enantioselectivity and more than 99% ee was obtained with **4a** at −25 °C in this procedure (Table 3, entries 9−11). The R in the ester group showed little effect on the enantioselectivity but had some effect on catalytic activity (Table 3, entries 10 and 12). The starting ligand **5** was also used in this amination, and both the catalytic activity and enantioselectivity were inferior to that resulting with **4a** (Table 3, entries 3 and 13).

From the asymmetric allylic substitutions mentioned above, ruthenocene ligands **4** showed much higher catalytic activity and higher enantioselectivity especially in asymmetric allylic alkylation than the corresponding ferrocene ligands **1**. It was also observed that R in the ester group had an effect on the asymmetric allylic substitutions, particularly on the asymmetric allylic alkylation. For ferrocene ligands **1**, **1b** with a larger group gave higher enantioselectivity than did **1a**. An opposite trend had been observed in the case of **4**.

Catalytic Test of Palladium-Catalyzed Asymmetric Allylic Substitution with Use of 12. Allylic acetate **12** is also a classical substrate in allylic substitution and has been extensively studied in the Pd-catalyzed system.[7i−n,10] Compared with allylic acetate **9**, fewer good results were attained for the palladium-catalyzed substitutions of allylic acetate **12**. Therefore, we also applied ligands **1** and **4** in the palladium-catalyzed substitutions of **12**. The reaction proceeded smoothly to give the corresponding cyclic allylation products **13** in good yields (88−94%) and enantioselectivities (60.5−81% ee) by using 2.5 mol % of the catalyst (Table 4).

(10) See reviews: (a) Trost, B. M.; Crawley, M. *Chem. Rev.* **2003**, *103*, 2921−2294. Selected papers: (b) Molander, G. A.; Burke, J. P.; Carroll, P. J. *J. Org. Chem.* **2004**, *69*, 8062−8069. (c) Ogasawara, M.; Ngo, H.; Sakamoto, T.; Takahashi, T.; Lin, W. *Org. Lett.* **2005**, *7*, 2281−2284. (d) Geisler, F.-M.; Helmchen, G. *J. Org. Chem.* **2006**, *71*, 2486−2492.

(11) Zhao, D. B.; Sun, J.; Ding, K. L. *Chem. Eur. J.* **2004**, *10*, 5952−5963.

(**a**: R=Me, **b**: R=Et)

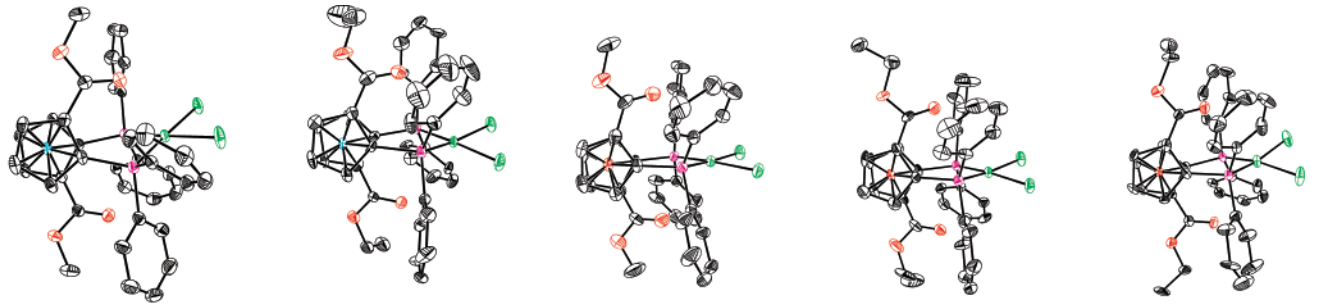
FIGURE 2. The structure of palladium complex **7** and **8**.

From Table 4, it was shown that the metal ion and/or R in the ester group had an effect on enantioselectivity in both asymmetric alkylation and amination reaction. In contrast with the asymmetric catalytic behavior mentioned above, ligand **4** with the larger R in the ester group resulted in higher enantioselectivity (Table 4, entries 1−4), and the opposite trend had also been observed with ligand **1** (Table 4, entries 5−8). The results combined with those obtained above indicated that the asymmetric catalytic behavior of **4** and **1** could be correlated to their structures, which encouraged us to further investigate their structure−property relationship in asymmetric catalysis.

X-ray Structures. To clarify the different effect on enantioselectivity with metal ions and R in the ester group mentioned above, a study of the crystal structures of **7** and **8** with palladium(II) was carried out. First, treating **4a** with 1 equiv of dichlorobis(acetonitrile)palladium(II) in benzene gave complex **7a** as one set of peaks in the ^{1}H NMR spectrum with quantitive yield (Figure 2). The corresponding complexes **7b**, **8a**, and **8b** were also prepared by using the same method (Figure 2). Then a single crystal of **7a** was obtained via crystallization from dichloromethane−petroleum ether. Others were also obtained from the component solvent in the same manner. Finally, the X-ray structures of **7** and **8** were determined (Figure 3). Similar to the configuration of complex **8a**, which was assigned by NOE determination before[4e] and proved by us here, complexes **7a**, **7b**, and **8b** also existed as configuration **2** and another possible configuration **3** was not found (Figure 1).

As expected, the twist angles of **7a** and **8a** are markedly different (23.63° in **7a** and 8.15° in **8a**, respectively, Figure 3) since the different distances between the two Cp rings (3.32 Å versus 3.68 Å) are as shown in Figure 1. In contrast to our presumption, **7a** has a larger twist angle than **8a** does, which was correlated to the leaning of the two Cp rings in **8a** (see the X-ray crystal structures in the Supporting Information). Next, we studied the effect of R group on the twist angle. The X-ray analysis of the single crystal of **8b** showed that two kinds of structures (A and B) existed in one crystal of **8b** with different twist angles (10.28° and 16.20°, Figure 3). Both twist angles are larger than that of **8a**. This is also possibly due to the angle between the two Cp rings in **8a** and **8b** (see the X-ray crystal structures in the Supporting Information). Different from the results of **8a** and **8b**, **7b** with a larger R in the ester group had a smaller twist angle (16.05°) than did **7a**.

From the results of the X-ray analysis and the palladium-catalyzed asymmetric allylic substitutions mentioned above, we found that the twist angle of the two Cp rings in the complexes clearly had an effect on enantioselectivity. For the palladium-catalyzed asymmetric allylic substitutions of **9**, the ligand with larger twist angle showed higher enantioselectivity, while an opposite trend had been observed for the asymmetric allylic substitution of **12**.



ORTEP view for twist angle (23.63°) of **7a** | ORTEP view for twist angle (16.05°) of **7b** | ORTEP view for twist angle (8.15°) of **8a** | ORTEP view for twist angle (10.28°) of **8b** (A) | ORTEP view for twist angle (16.20°) of **8b** (B)

FIGURE 3. Comparison of the molecular structures of **7** and **8**.

Conclusion

In summary, we have prepared the novel C_2-symmetric planar chiral diphosphine ligands **4** and applied them in the palladium-catalyzed asymmetric allylic substitutions. Good to excellent enantioselectivities, especially much higher catalytic activities, were observed in asymmetric allylic alkylation and amination. Compared to the corresponding ferrocene ligands **1**, a different effect of R in the ester group on enantioselectivity was observed. For ruthenocene ligands **4**, the one with a smaller R in the ester group had higher enantioselectivity for the palladium-catalyzed asymmetric allylic substitutions of **9**. An opposite trend was observed with **1**. However, for the palladium-catalyzed asymmetric allylic substitution of **12**, ligand **4** with a larger group resulted in somewhat higher enantioselectivity instead. The X-ray study on the Pd(II) complex of **4** and **1** had been carried out. The results that ligand **4** and its analogue **1** showed an opposite trend on enantioselectivities varying with R in the ester group might possibly account for their opposite trend of the corresponding twist angle. It could be deduced that the twist angle in the metallocene diphosphine ligands with only planar chirality had a pivotal influence on the asymmetric allylic substitutions.

Experimental Section

Ester Amide (6). To a solution of compound **5** (1.65 g, 2.0 mmol) in THF (40 mL) were added water (2 mL), trifluoroacetic acid (3.8 mL, 49 mmol), and Na_2SO_4 (18.8 g), and this suspension was stirred overnight at room temperature. After filtration and removal of the solvent under reduced pressure, a mixture containing unstable ester ammonium salt was obtained as a brown solid. To a solution of this ester ammonium salt in dichloromethane (40 mL) were added pyridine (7.2 mL, 89 mmol) and acetic anhydride (12.0 mL, 76 mmol), and the mixture was stirred at room temperature overnight. The mixture was washed with 1 N HCl, water, and then brine and dried over Na_2SO_4. After removal of the solvent, the residue obtained was purified by silica gel column chromatography with ethyl acetate as an eluent to afford pure ester amide **6** as a light green solid (1.56 g, 83% overall yield from **5**). Mp 219−220 °C. $[\alpha]^D_{27}$ −359.3 (*c* 0.91, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 Hz) δ 0.97 (d, J = 6.4 Hz, 6H), 1.01 (d, J = 6.4 Hz, 6H), 1.87 (s, 6H), 1.98 (m, 2H), 3.82 (br s, 2H), 3.90 (t, J = 8.8 Hz, 2H), 4.04 (dd, J = 11.6 Hz, 2.8 Hz, 2H), 4.37 (dd, J = 10.8, 2.8 Hz), 4.84 (br s, 2H), 5.38 (br s, 2H), 6.50 (d, J = 8.8 Hz 2H), 7.13−7.32 (m, 20H); ^{13}C NMR ($CDCl_3$, 100 Hz) δ 19.3, 19.8, 23.4, 29.5, 53.5, 65.8, 78.1, 80.2, 80.3, 81.3, 81.9, 82.0, 83.9, 84.1, 128.31, 128.36, 128.71, 128.78, 128.8, 129.6, 132.1, 132.3, 134.4, 134.6, 136.5, 136.6, 138.4, 138.5, 168.9, 169.0, 170.3; ^{31}P NMR ($CDCl_3$, 162 Hz, 85% H_3PO_4) δ −16.15; MS (MALDI) *m*/*z* 943 [M + 1$^+$] (100); HRMS calcd for $C_{50}H_{55}N_2O_6P_2Ru$ 943.2573, found 943.2592.

(−)-(*S*)-(*S*)-1,1′-Bis(diphenylphosphino)-2,2′-bis(methoxycarbonyl)ruthenocene (4a). To a solution of ester amide **6** (0.53 g, 0.56 mmol) in THF (10 mL) was added a sodium methoxide solution prepared by the addition of sodium metal (0.52 g, 22 mmol) to methanol (35 mL). After being stirred for 24 h, the mixture was neutralized with methanolic acetic acid, and the solvent was removed by evaporation. The residue was dissolved in dichloromethane (60 mL), and the solution was washed with water and then brine and dried over Na_2SO_4. After removal of the solvent, the residue was purified by silica gel column chromatography with petroleum ether−ethyl acetate (4:1) as an eluent to afford **4a** as a light green solid (0.30 g, 75%). Mp 242−244 °C. $[\alpha]^D_{27}$ −513.9 (*c* 0.61, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 Hz) δ 3.70 (s, 6H), 3.87 (br s, 2H), 4.68 (br s, 2H), 5.43 (br s, 2H), 7.21−7.30 (m, 20H); ^{13}C NMR ($CDCl_3$, 100 Hz) δ 51.8, 79.3, 79.3, 79.4, 82.5, 82.7, 85.4, 85.6, 128.1, 128.2, 128.4, 128.5, 128.53, 129.1, 132.4, 132.6, 134,5, 134,8, 137.7, 137.8, 139.0, 139.1, 168.80, 168.82; ^{31}P NMR ($CDCl_3$, 162 Hz, 85% H_3PO_4) δ −17.18; MS (MALDI): *m*/*z* 717 [M + 1$^+$] (100); HRMS calcd for $C_{38}H_{33}O_4P_2Ru$ 717.0892, found 717.0922.

(−)-(*S*)-(*S*)-1,1′-Bis(diphenylphosphino)-2,2′-bis(ethoxycarbonyl)ruthenocene (4b). Following a procedure identical with that described for the preparation of **4a**, the reaction of **6** (0.34 g, 0.36 mmol) in THF (10 mL) with a sodium ethoxide solution prepared by the addition of sodium metal (0.60 g, 25 mmol) to ethanol (20 mL) for 48 h afforded **4b** as a yellow solid (0.20 g, 74%). Mp 229−231 °C. $[\alpha]^D_{27}$ −409.8 (*c* 0.78, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 Hz) δ 1.12 (t, J = 6.8 Hz, 6H), 3.83 (br s, 2H), 4.08−4.15 (m, 2H), 4.19−4.25 (m, 2H), 4.76 (br s, 2H), 5.42 (br s, 2H), 7.18−7.30 (m, 20H); ^{13}C NMR ($CDCl_3$, 100 Hz) δ 14.3, 60.8, 77.0, 79.5, 79.6, 82.7, 82.9, 84.9, 85.1, 128.1, 128.2, 128.4, 128.5, 129.0, 132.4, 132.6, 134.5, 134.7, 137.7, 137.8, 139.0, 139.1, 168.4, 168.5; ^{31}P NMR ($CDCl_3$, 162 Hz, 85% H_3PO_4) δ −17.00; MS (MALDI) *m*/*z* 745 [M + 1$^+$] (100); HRMS calcd for $C_{40}H_{37}O_4P_2Ru$ 745.1025, found 745.1180.

[$PdCl_2$(4a)] (7a). A suspension of **4a** (33.5 mg, 0.05 mmol) and dichlorobis(acetonitrile)palladium (13.0 mg, 0.05 mmol) in dry benzene (2 mL) was stirred under nitrogen for 1 h to produce a precipitate. After the solvent was removed, **7a** was obtained as a yellow solid in quantitive yield. Recrystallization of **7a** from dichloromethane−petroleum ether provided yellow prismatic crystals, which contain one molecule of dichloromethane per complex as determined by ^{1}H NMR and single crystal analysis. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.41 (s, 6H), 4.76 (m, 4H), 5.21 (t, J = 2 Hz, 2H), 5.29 (s, 1H, CH_2Cl_2), 7.40−7.42 (m, 12H), 8.06−8.10 (m, 4H), 8.13−8.18 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 Hz) δ 52.4, 75.0, 76.6, 80.2, 85.76, 98.7, 98.9, 127.5, 127.6, 127.7, 128.2, 128.3, 128.4, 130.7, 131.0, 135.1, 135.2 136.1, 136.2, 137.3, 167.9; ^{31}P NMR ($CDCl_3$, 162 Hz, 85% H_3PO_4) δ 42.02.

[PdCl$_2$(4b)] (7b). Following a procedure identical with that described for the preparation of **7a**, Recrystallization of **7b** from ethyl acetate−carbon tetrachloride provided yellow prismatic crystals. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.97 (t, J = 6.8 Hz, 6H), 3.92 (m, 4H), 4.74 (br s, 2H), 4.75 (br s, 2H), 5,19 (br s, 2H), 7.36−7.41 (m, 12H), 8.04−8.06 (m, 4H), 8.16−8.18 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 Hz) δ 14.3, 61.5, 74.9, 76.3, 80.6, 85.5, 97.9, 98.2, 127.2, 127.3, 127.4, 128.1, 128.2, 128.3, 130.4, 130.8, 135.2, 135.3, 135.4, 136.41, 136.46, 136.5, 167.0; ^{31}P NMR ($CDCl_3$, 162 Hz, 85% H_3PO_4) δ 40.79.

[PdCl$_2$(1a)] (8a). Following a procedure identical with that described for the preparation of **7a**, recrystallization of **8a**[4a,e] from dichloromethane−petroleum ether provided red-brown crystals.

[PdCl$_2$(1b)] (8b). Following a procedure identical with that described for the preparation of **7a**, recrystallization of **8b** from dichloromethane−ethyl acetate−petroleum ether provided red-brown crystals. It was found that two kinds of structures (A and B) existed in one crystal. However, this crystal gave only one set of peaks in ^{1}H NMR spectrum in $CDCl_3$ solution. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.94 (t, J = 7.2 Hz, 6H), 3.85 (q, J = 7.2 Hz, 4H), 4.24 (br s, 2H), 4.47 (br s, 2H), 4.75 (br s, 2H), 5.29 (s, 1H, CH_2Cl_2), 7.34−7.40 (m, 12H), 8.06−8.14 (m, 4H), 8.20−8.32 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 Hz) δ 14.3, 61.5, 68.3, 72.3, 73.6, 84.4, 96.44, 96.47, 127.40, 127.45, 127.5, 128.0, 128.1, 128.2, 130.5, 130.9, 135.63, 135.67, 135.7, 136.4, 136.5, 136.6, 168.0; ^{31}P NMR ($CDCl_3$, 162 Hz, 85% H_3PO_4) δ 45.60.

General Procedure for Palladium-Catalyzed Asymmetric Allylic Alkylation (10). A mixture of ligand (30 μmol) and [Pd(η^3-C_3H_5)Cl]$_2$ (4.60 mg, 12.5 μmol) in dry dichloromethane (1 mL) was stirred at room temperature under nitrogen for 1 h, and the resulting green solution was added to a mixture of **9** (0.252 g, 1.00 mmol) and potassium acetate (0.0020 g, 20 μmol) in dry dichloromethane (2 mL) via a cannula, followed by the addition of dimethyl malonate (0.396 g, 3.00 mmol) and BSA (0.613 g, 3.00 mmol). The reactions were carried out at room temperature and monitored by TLC for the disappearance of **9**. When **9** disappeared, the solvent was evaporated and the resulting mixture was extracted with ether (20 mL). The extract was washed twice with ice-cold saturated NH_4Cl aqueous solution (25 mL) and then dried over Na_2SO_4. After removal of the ether, the residue was purified on silica gel column chromatography with hexane−ethyl acetate (8:1) to afford pure product **10**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.51 (s, 3H), 3.69 (s, 3H), 3.94 (d, J = 10.8 Hz, 1H), 4.25 (dd, J = 8.8, 10.8 Hz, 1H), 6.32 (dd, J = 8.4, 15.6 Hz, 1H), 6.46 (d, J = 15.6 Hz, 1H), 7.17−7.32 (m, 10H); the enantiomeric excess was determined by HPLC on a Chiralpak OD-H column.

General Procedure for Palladium-Catalyzed Asymmetric Allylic Amination (11). A solution of [PdCl(η^3-C_3H_5)]$_2$ (1.8 mg, 0.005 mmol) and the ligand (0.011 mmol) in dichloromethane (1 mL) was stirred for 1 h under nitrogen before use. Subsequently, a solution of **9** (126 mg, 0.5 mmol) in dichloromethane (1.5 mL) and benzylamine (131 μL, 1.5 mmol) was added. The reactions were carried out at room temperature and monitored by TLC for the disappearance of **9**. When **9** disappeared, the reaction mixture was diluted with Et_2O (5 mL) and washed with saturated NH_4Cl (aq) (25 mL). The aqueous phase was extracted with ethyl ether (5 mL) and the combined organic phase was washed with brine then dried over Na_2SO_4. After removal of the ether, the residue was purified on silica gel column chromatography with hexane−ethyl ether (10:1) to afford pure product **11**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.75−3.81 (m, 2H), 4.41 (d, J = 7.6 Hz, 1H), 6.32 (dd, J = 7.6, 15.6 Hz, 1H), 6.58 (d, J = 16 Hz, 1H), 7.21−7.44 (m, 15H) ppm; the enantiomeric excess was determined by HPLC on a Chiralcel OJ-H column.

General Procedure for Palladium-Catalyzed Asymmetric Allylic Alkylation (13a). Compound **13a** was prepared in 90−94% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26−1.80 (m, 4 H), 1.96−2.01 (m, 2H), 2.87−2.93 (m, 1H), 3.29 (d, J = 9.2 Hz, 1H), 3.73 (s, 3 H), 3.74 (s, 3 H), 5.52 (ddd, J = 2.4, 4.0, 10 Hz, 1H), 5.75−5.80 (m, 1H); the enantiomeric excess was determined by HPLC on a Chiralcel AD-H column.

General Procedure for Palladium-Catalyzed Asymmetric Allylic Amination (13b). Compound **13b** was prepared in 86−89% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.45−2.04 (m, 6 H), 3.19−3.25 (m, 1H), 3.80−3.89 (dd, J = 13.2, 18.8 Hz, 2H), 5.71−5.80 (m, 2H), 7.22−7.36 (m, 5H); the enantiomeric excess was determined by HPLC on a Chiralcel AD-H column.

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Supporting Information Available: Experimental procedures, spectroscopic data for all new compounds, the CIF files for all X-rays structures, and characterization data for products of asymmetric allylic substitutions. This material is available free of charge via the Internet at http://pubs.acs.org.

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